

What we claim is:

1. A method for identifying an interacting set of molecules comprising:

A) generating fragments of a reporter molecule which have a directly or indirectly

5 detectable activity when associated;

B) coupling first fragments of said reporter molecule to members of a first panel of molecules;

C) coupling second fragments of said reporter molecule to members of a second panel of molecules;

10 D) mixing the products of B) and C);

E) directly or indirectly testing for said reporter molecule activity; and

F) identifying the panel members whose interaction resulted in said reporter molecule activity and which thus form an interacting set.

15 2. A method for identifying an interacting set of molecules comprising:

A) identifying a first panel and a second panel of molecules whose mutual interaction is desired to be tested;

B) coupling molecules of said first panel to first fragments of a reporter molecule;

C) coupling molecules of said second panel to second fragments of said reporter

20 molecule;

D) mixing the products of B) and C);

E) directly or indirectly testing for said reporter molecule activity; and

F) identifying the panel members whose interaction resulted in said activity and which thus form an interacting set.

3. A method of screening multiple panels of molecules against each other to determine the ability of individual panel members to interact with each other, said method comprising:

A) coupling first fragments and second fragments of a reporter molecule to different panel members;

B) mixing the products of A);

C) testing for said reporter molecule activity; and

D) identifying the panel members whose interaction results in said reporter molecule activity and which thus form interacting members.

4. A method according to any of Claims 1-3 where at least two of said panels comprise a library of molecules.

5. A method according to any of Claims 1-3 where at least one of said panels comprises a library of molecules.

6. A method comprising directly or indirectly introducing different interacting sets into separate cell populations and identifying an interacting set that provides its host cells with a growth advantage relative to cells containing a different set.

7. A method comprising directly or indirectly introducing different interacting sets into separate cell populations and identifying an interacting set that provides its host cells with a quantifiable signal that is greater than the signal generated by a different set.

5 8. A method of preparing an assay system comprising:

A) identifying a first panel of molecules and a second panel of molecules whose mutual interaction is desired to be tested;

B) coupling molecules of said first panel to first fragments of a reporter molecule; and

C) coupling molecules of said second panel to second fragments of said reporter
10 molecule.

9. An assay system comprising a first panel of molecules coupled to first fragments of a reporter molecule and a second panel of molecules coupled to second fragments of said reporter molecule.

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10. A composition comprising at least one compound produced according to step B) of Claim 8 and at least one compound produced according to step C) of Claim 8.

11. A method for identifying interacting molecules comprising:

20 (A) generating fragments of a reporter molecule, said fragments having a directly or indirectly detectable activity when associated;

(B) coupling first fragments of said reporter molecule to members of a panel of molecules;

(C) coupling a second fragment of said reporter molecule to a second molecule;

(D) mixing the products of B) and C);
(E) directly or indirectly testing for said reporter molecule activity; and
(F) identifying the panel members whose interaction with said second molecule resulted in said reporter molecule activity.

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12. A method for identifying interacting molecules comprising:

(A) identifying a panel of molecules and identifying a second molecule whose interaction with members of said panel is desired to be tested;

(B) coupling members of said panel to first fragments of a reporter molecule;

10 (C) coupling the second molecule to a second fragment of said reporter molecule;

(D) mixing the products of B) and C);

(E) directly or indirectly testing for said reporter molecule activity; and

(F) identifying the panel members whose interaction with said second molecule resulted in said reporter molecule activity and which thus form interacting molecules.

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13. A method of screening a first molecule against a panel of molecules to determine the ability of said first molecule to interact with individual members of said panel comprising:

A) coupling a first fragment of a reporter molecule to said first molecule;

20 B) coupling second fragments of said reporter molecule to different members of said panel;

C) mixing the products of A) and B);

D) testing for said reporter molecule activity; and

E) identifying the members of said panel whose interaction with said first molecule results in said reporter molecule activity and which thus interact with said first molecule.

14. A method according to any of Claims 11-13 wherein said panel comprises a library of molecules.

5 15. A method comprising directly or indirectly introducing different interacting molecules into separate cell populations and identifying those interacting molecules that provide their host cells with a growth advantage relative to cells containing different molecules.

10 16. A method comprising directly or indirectly introducing different interacting molecules into separate cell populations and identifying those interacting molecules that provides their host cells with a quantifiable signal that is greater than the signal generated by different molecules.

15 17. A method of preparing an assay system comprising: (A) identifying a panel of molecules whose interactions with a second molecule are desired to be tested; (B) coupling members of said panel to first fragments of a reporter molecule; and (C) coupling said second molecule to a second fragment of said reporter molecule.

18. An assay system comprising a panel of molecules coupled to first fragments of a reporter molecule and a second molecule coupled to a second fragment of said reporter molecule.

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19. A composition comprising at least one compound produced according to step B) of Claim 17 and at least one compound produced according to step C) of Claim 17.

20. A method for identifying interacting molecules comprising: (A) generating fragments of a reporter molecule which have a directly or indirectly detectable activity when associated; (B) coupling a first fragment of said reporter molecule to a first molecule; (C) coupling a second fragment of said reporter molecule to a second molecule; (D) mixing the products of B) and C);
5 and (E) directly or indirectly testing for said reporter molecule activity in the absence or presence of one or more chemical or biological compounds.

21. A method for identifying interacting molecules comprising:

A) identifying a first molecule and a second molecule whose interaction is desired to be
10 tested;

B) coupling said first molecule to a first fragment of a reporter molecule;

C) coupling said second molecule to a second fragment of said reporter molecule;

D) mixing the products of B) and C);

E) directly or indirectly testing for said reporter molecule activity.

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22. A method according to any of Claims 1-3 and Claims 11-13 and Claims 20-21 wherein fragments are used that have decreased avidity for each other relative to a reference set of fragments.

20 23. A method according to any of Claims 1-3 and Claims 11-13 and Claims 20-22 wherein fragments are used that produce a detectable signal that is higher than that of a reference set of fragments.

24. A method of preparing an assay system comprising:

A) identifying a first molecule and a second molecule whose interaction is desired to be tested;

B) coupling said first molecule to a first fragment of a reporter molecule; and

C) coupling said second molecule to a second fragment of said reporter molecule.

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25. An assay system comprising a first molecule coupled to a first fragment of a reporter molecule and a second molecule coupled to a second fragment of said reporter molecule.

26. A composition comprising at least one compound produced according to step B) of

10 Claim 24 and at least one compound produced according to step C) of Claim 24.

27. A composition comprising one or more interacting molecules as identified by a method according to any of Claims 1-8, 11-17 and 20-24.

15 28. Cells containing interacting molecules as identified by a method according to any of Claims 1-8, 11-17 and 20-24.

29. A method according to any of Claims 1-5, 8-9, 11-18, 20, 21, 24 and 25 wherein said molecules are nucleic acids, peptides, or proteins.

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30. A method according to any of Claims 1-3, 8-9, 11-14, 17-18, 20-22 and 24-25 wherein said reporter molecule generates an optically detectable signal.

31. A method according to any of Claims 1-3, 8-9, 11-14, 17-18, 20-22 and 24-25 wherein said reporter molecule generates a fluorescent, luminescent, or phosphorescent signal or a color.

5 32. A method according to any of Claims 1-3, 8-9, 11-14, 17-18, 20-22 and 24-25 wherein said reporter molecule generates a signal that can be quantified within living cells.

33. A method according to any of Claims 1-3, 8-9, 11-14, 17-18, 20-22 and 24-25 wherein said reporter molecule generates a signal that can be localized within living cells.

10 34. A method according to any of Claims 1-3, 8-9, 11-14, 17-18, 20-22 and 24-25 wherein said reporter molecule generates a drug resistance activity.

35. A method according to any of Claims 1-3, 8-9, 11-14, 17-18, 20-22 and 24-25
15 wherein said reporter molecule allows cell survival.

36. A method according to any of Claims 1-3, 8-9, 11-14, 17-18, 20-22 and 24-25 wherein the reporter molecule is selected from the group consisting of a selectable marker, a drug resistance marker, an antibody, an antigen, a monomeric enzyme, a fluorescent protein, a
20 luminescent protein, and a phosphorescent protein.

37. A method according to any of Claims 1-3, 8-9, 11-14, 17-18, 20-22, and 24-25 wherein the reporter molecule activity is detected by a one or more methods selected from the group consisting of: cell number, cell density, cell size, cell shape, colony formation, cell DNA

quantity, cell protein quantity, cell staining, cell color, fluorescence, optical density, luminescence, phosphorescence, spectroscopy, flow cytometry, microscopy, or image analysis.